

Office Action Summary**Application No.**

10/571,291

Applicant(s)

GAILLARD ET AL.

ExaminerVENKATARAMAN
BALASUBRAMANIAN**Art Unit**

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2010.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 10-14 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-8 and 10-14 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Applicants' response, filed on 12/22/2010, is made of record. Claims 1-8 and 10-14 are pending. In view of applicants' assertion that Gaillard is commonly owned, the 103 rejection over Gaillard et al., W003/091249 in view of Bennett (or Kaneto-I, Kaneto-II, Kaneto-III or Hotamisliligil) and Gatlin or Fine, US 6,376,549, made in the previous office action has been obviated. However, the following rejection made in the previous office action is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Halazy et al., WO 01/47920 in view of Bennett et al., Current Opinion in Pharmacology 2003, 3:420-425(or Kaneto-I, Kaneto-II, Kaneto-III or Hotamisligil) and Gatlin et al., US 6,559,188 .

This rejection is same as made in the previous office action and is maintained for reasons of record.

Applicants' traversal to overcome this rejection is not persuasive.

Applicants have argued that Kaneto-I, Kaneto-II, Kaneto-III or Hotamisligil are not prior art. This is not entirely correct. The cited references are review articles which relate role of Janus kinase in diabetes and they provided number of references which earlier than instant effective priority date.

For example, Kaneto-I, teaches the role of JNK and its inhibitors in diabetes in pages 431-432 citing references 62-77 and Kaneto-II teaches the role of JNK and its inhibitors in diabetes in pages 581-585 citing references 8-89 and Kaneto-III teaches the role of JNK and its inhibitors in diabetes in pages 167-174 citing references 65-84. Hotamisligil also teaches the role of JNK and its inhibitors in diabetes in pages 167-174 citing references 65-84. All these references are prior art.

In addition, applicants' assertion that Kaneto-III is published online in 2005 is not

persuasive. The fact that the 2004 article is subsequently published online in 2005 does not invalid date the original hard copy publication.

In short, the compounds taught by Halazy are same as that of instant claims. Instant specification on page 2 clearly acknowledges this. The compounds of Halazy are JNK inhibitors. Thus, administering the genus of compounds of Halazy (that is instant genus of compounds) would inhibit JNK. Whatever negative attributes applicants offer for method of use of compounds of Halazy would be equally applicable to instant compounds.

Bennett et al., clearly teaches JNK inhibitors to be useful in treating insulin resistance, diabetes and obesity as seen pages 420-422. Instant claims recite the same. Applicants argued, pointing page that while instant compounds decreases insulin and glucose, Bennett teaches lowering of plasma glucose but not plasma insulin. This is not correct. Contrary to applicants' urging, the Figure 2 shown in page 422 of Bennett clearly shows lowering of plasma glucose and insulin. And it is also improper comparison as applicants have measured plasma glucose level and plasma insulin level after 4 hr as pointed by applicants(see page 29, lines 18-21).

Thrust of applicants' argument is that Bennett's compound increase insulin level, based on the data 20 ng to 30 ng during first 15 minutes of administration, while instant compounds decrease insulin level. However, as seen in Figure 2, Bennett teaches decrease in insulin level at 120 minutes. Applicants have not shown that instant compound does not raise initial insulin level before decreasing. Applicants' measurement of insulin level appears to be at 4hrs after administration of the instant

compound.

Contrary to applicants' urging pointing column 1 of page 422, Bennett in this column clearly teaches usefulness of JNK inhibitors in treating insulin resistance, diabetes and obesity as reproduced below:

"We have studied the performance of a small molecule JNK inhibitor (Celgene Corporation; CC105) in the leptin-receptor-deficient model of diabetes and obesity, the db/db mouse. This strain exhibits an early-phase hyper- insulinemia followed by progressive pancreatic failure and hypoinsulinemia from about six weeks of age. This leads to increased blood glucose and obesity. After 17 days of oral dosing with the JNK inhibitor, we observed significantly lower blood glucose and higher insulin levels (Figure 2). After oral glucose loading, we observed increased plasma insulin and improved glucose control in animals treated with the JNK inhibitor (Figure 2). Ex vivo analysis of pancreatic islet cells showed marked improvements in acinar recovery and morphology, as well as insulin release following high glucose stimulation (Figure 3). This preliminary pharmacological data shows striking parallels to the observations made using Jnk1-l- ob/ob mice. Further studies in appropriate models should define the potential of JNK inhibitors in treating insulin resistance and obesity".

Clearly, based on the significant lowering of blood sugar, one would expect JNK inhibitors to be useful for treating Type-II diabetes and obesity. The entire document and especially the concluding paragraph clearly lend support for JNK inhibitors to treat diabetes, insulin resistance and obesity. It is held that, although there is no reason to doubt the compounds of Halazy were not useful for treating insulin resistance, even if

they were not useful for treating insulin resistance, the compounds of Halazy would be useful for treating diabetes and obesity.

It should also be noted that applicants' argument that instant compounds lower insulin and hence useful for treating metabolic disorders claimed therein is also not persuasive for another reason. Method of use claims 9 and 10 clearly recites use of additional insulin selected from group consisting of a rapid acting insulin, an intermediate acting insulin, a long acting insulin, a combination of intermediate and rapid acting insulins. Thus, applicants first argues that Bennett's compounds raise insulin levels while instant compounds do not and then for the actual method of use applicants states additional insulin is needed to be effectively treat claimed metabolic disorders. This is clearly contradictory to applicants' criticisms of Bennett. Hence, it appears that the decreasing insulin level appears to be not critical. Thus, Bennett et al., teaches JNK inhibitors to be useful in treating insulin resistance, diabetes and obesity.

Similarly, the all the secondary references Kaneto-I, Kaneto-II, Kaneto-III and Hotamisligil teach usefulness of JNK inhibitors for treating Type-II diabetes. See entire document.

In addition, method of use claims recites additional active ingredients for a combination therapy.

Again, it is known at the time of instant invention the effectiveness of treatment of diabetes can be increased by using a combination of antidiabetic agents.

For example, Gatlin teaches use combination of various anti-diabetic agents including PPAR gamma agonists claimed in the currently amended claims. See entire

document. Especially, see column 1-5, 11-14 and 21-22 for combination of active ingredients for treating diabetes.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made based on to combined the teaching of Gaillard and Bennett to make various compounds of formula I as permitted by the reference using teachings of Gaillard, and expect resulting compounds to possess the uses taught by the combined art in combination therapy in view of the equivalency teaching outline above.

For reasons stated above this rejection is proper and is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571)

272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624